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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/527,647	08/01/2005	Johan Andersson	026220-00064	7625
4372	7590	03/20/2008		
ARENT FOX LLP 1050 CONNECTICUT AVENUE, N.W. SUITE 400 WASHINGTON, DC 20036			EXAMINER KOSACK, JOSEPH R	
			ART UNIT 1626	PAPER NUMBER
			NOTIFICATION DATE 03/20/2008	DELIVERY MODE ELECTRONIC

**Please find below and/or attached an Office communication concerning this application or proceeding.**

The time period for reply, if any, is set in the attached communication.

Notice of the Office communication was sent electronically on above-indicated "Notification Date" to the following e-mail address(es):

DCIPDocket@arentfox.com  
IPMatters@arentfox.com  
Patent\_Mail@arentfox.com

<b>Office Action Summary</b>	<b>Application No.</b> 10/527,647	<b>Applicant(s)</b> ANDERSSON ET AL.	
	<b>Examiner</b> Joseph R. Kosack	<b>Art Unit</b> 1626	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

### Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

### Status

- 1) ☒ Responsive to communication(s) filed on 17 January 2008.
- 2a) ☐ This action is **FINAL**.                      2b) ☒ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

### Disposition of Claims

- 4) ☒ Claim(s) 1,7-22,24,32,34,35,39-45 and 50 is/are pending in the application.
- 4a) Of the above claim(s) 32,34 and 35 is/are withdrawn from consideration.
- 5) ☐ Claim(s) \_\_\_\_\_ is/are allowed.
- 6) ☒ Claim(s) 1,7-22,24,39-45 and 50 is/are rejected.
- 7) ☐ Claim(s) \_\_\_\_\_ is/are objected to.
- 8) ☐ Claim(s) \_\_\_\_\_ are subject to restriction and/or election requirement.

### Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on \_\_\_\_\_ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.  
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).  
Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

### Priority under 35 U.S.C. § 119

- 12) ☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☒ All    b) ☐ Some \*    c) ☐ None of:
- ☐ Certified copies of the priority documents have been received.
  - ☐ Certified copies of the priority documents have been received in Application No. \_\_\_\_\_.
  - ☒ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

\* See the attached detailed Office action for a list of the certified copies not received.

### Attachment(s)

- |  |   |
|--|---|
| 1) <input type="checkbox"/> Notice of References Cited (PTO-892)                     | 4) <input type="checkbox"/> Interview Summary (PTO-413)           |
| 2) <input type="checkbox"/> Notice of Draftsperson's Patent Drawing Review (PTO-948) | Paper No(s)/Mail Date. _____                                      |
| 3) <input type="checkbox"/> Information Disclosure Statement(s) (PTO/SB/08)          | 5) <input type="checkbox"/> Notice of Informal Patent Application |
| Paper No(s)/Mail Date _____  | 6) <input type="checkbox"/> Other: _____                          |

### **DETAILED ACTION**

Claims 1, 7-22, 24, 32, 34-35, 39-45, and 50 are pending in the instant application.

#### ***Continued Examination Under 37 CFR 1.114***

A request for continued examination under 37 CFR 1.114, including the fee set forth in 37 CFR 1.17(e), was filed in this application after final rejection. Since this application is eligible for continued examination under 37 CFR 1.114, and the fee set forth in 37 CFR 1.17(e) has been timely paid, the finality of the previous Office action has been withdrawn pursuant to 37 CFR 1.114. Applicant's submission filed on January 17, 2008 has been entered.

#### ***Previous Claim Rejections - 35 USC § 103***

Claims 1, 7-22, 24 and 39-45 were previously rejected under 35 U.S.C. 103(a) as being unpatentable over Del Soldato et al. (WO 95/30641 A1) in view of Lai et al. (USPN 6,355,666), Cainelli et al. (*J. Chem. Soc. Perkin Trans.*, 1987, 2637-2642) and Hwu et al. (*Synthesis*, 1994, 471-474).

Applicant has traversed the rejection on the grounds that Hwu et al. teach away from lowering the reaction temperature. This is not found to be persuasive because the numbers that Applicant puts forth in its summary of Hwu et al. are a combination of different sulfonates for each group. Hwu et al. disclose only one temperature for each sulfonate tested. Applicant is attempting to compare apples to oranges by broadly combining the reaction runs of Hwu et al. of sulfonates of various functionalities to

Art Unit: 1626

attempt to build a picture on conversion rates. Therefore, Hwu et al. do not teach away from lowering the temperature and it is still considered to be routine optimization.

Applicant has also submitted a declaration by Romano Rivolta under 37 CFR 1.132 executed November 6, 2007 that shows an increase in impurities as temperature increases. However, the data set presented does not show any reactions done at temperatures higher than 90° C. Therefore, it seems as if the data set is incomplete and the Examiner disagrees with the extrapolation that the Rivolta declaration provides. Additional data points in the extrapolated region above 85° C would be needed to show that impurities drastically increase with the increased temperature. Therefore, the rejections must currently be maintained.

### ***Claim Rejections - 35 USC § 103***

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negated by the manner in which the invention was made.

The factual inquiries set forth in *Graham v. John Deere Co.*, 383 U.S. 1, 148 USPQ 459 (1966), that are applied for establishing a background for determining obviousness under 35 U.S.C. 103(a) are summarized as follows:

1. Determining the scope and contents of the prior art.
2. Ascertaining the differences between the prior art and the claims at issue.
3. Resolving the level of ordinary skill in the pertinent art.
4. Considering objective evidence present in the application indicating obviousness or nonobviousness.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

Claims 1, 7-22, 24, 39-45, and 50 are rejected under 35 U.S.C. 103(a) as being unpatentable over Del Soldato et al. (WO 95/30641 A1) in view of Lai et al. (USPN 6,355,666), Cainelli et al. (*J. Chem. Soc. Perkin Trans.*, 1987, 2637-2642) and Hwu et al. (*Synthesis*, 1994, 471-474).

The instant application is drawn to a process for making a nitrooxy linked diclofenac. The process comprises reacting diclofenac with a diol-linker, reacting the resulting product with an alkylsulfonyl source, and reacting that product with an alkali nitrate to yield the final product. Exact details on solvents, purification, and other parameters are provided in the claims.

*Determination of the scope and content of the prior art (MPEP §2141.01)*

Del Soldato et al. teach the reaction of diclofenac with a dihalolinker (either alkyl or ether linker) with further reaction with silver nitrate to yield the nitrooxy-linked diclofenac. See pages 40-51.

Ascertainment of the difference between the prior art and the claims (MPEP §2141.02)

Del Soldato et al. do not teach the reaction of diclofenac with a glycol linker, reaction of that product with an alkylsulfonyl source, or reaction with an alkali nitrate. Also, the exact details of solvents, purification, and other parameters provided in dependent claims are not addressed.

Finding of prima facie obviousness--rational and motivation (MPEP §2142-2413)

Lai et al. teach the reaction of NSAID's, such as diclofenac and naproxen, with glycolic linkers in chloroform and toluenesulfonic acid. See columns 9-15.

Cainelli et al. teach the reaction of a hydroxyl group with mesityl chloride in triethylamine and toluene to yield a methanesulfonyl compound. Further reaction with tetrabutylammonium nitrate yields a nitrooxy compound. See page 2641, Compounds 8-11.

Hwu et al. teaches using a mixture of tetrabutylammonium nitrate and sodium nitrate for the nitration step. See page 472.

The remaining differences in solvents, acids, crystallization, alkali metal nitrate source, and temperature are deemed to be routine experimentation. The above items are either routinely modified in the art to affect yield and crude purity of a reaction (solvent, acid, and temperature) or is a step that is routinely performed to purify a compound (crystallization.) "[W]here the general conditions of a claim are disclosed in the prior art, it is not inventive to discover the optimum or workable ranges by routine experimentation." In re Aller, 220 F.2d 454, 456, 105 USPQ 233, 235 (CCPA 1955)

Therefore, it would have been obvious to one of ordinary skill in the art at the time the claimed invention was made to modify the reaction scheme of Del Soldato et al. with the guidance of Lai et al., Cainelli et al., and Hwu et al. along with routine experimentation to make the claimed invention with a reasonable expectation of success. The motivation to do so is to reduce the cost of manufacturing nitrooxy-linked diclofenac which has been known for over a decade.

Thus, the claimed invention as a whole was *prima facie* obviousness over the combined teachings of the prior art.

### ***Conclusion***

Claims 1, 7-22, 24, 39-45, and 50 are rejected.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Joseph R. Kosack whose telephone number is (571)272-5575. The examiner can normally be reached on M-Th 6:30-5:00.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Joseph McKane can be reached on (571)-272-0699. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Art Unit: 1626

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see <http://pair-direct.uspto.gov>. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

/Kamal A Saeed, Ph.D./  
Primary Examiner, Art Unit 1626

/Joseph R Kosack/  
Examiner, Art Unit 1626